In the Claims:

The current status of all claims is listed below and supercedes all previous lists of claims.

Please cancel claims 112, 114-120, 127-156, and 159-164 without prejudice to their presentation in another application as being drawn to a non-elected invention.

Please cancel claims 95, 96, 101-104, 106, 107, 113, 121, 124, and 157 without prejudice to their presentation in another application.

Please amend claims 94, 105, 123, 125, 126, and 158 as follows:

1-93. (cancelled).

94. (currently amended) A method of modification of a target RNA comprising contacting the target RNA with a double stranded RNA having first and second strands, said first strand comprising at least four consecutive 2'-hydroxyl ribonucleosides and at least one modified nucleoside;

the first and second strands being hybridized to each other, wherein the first and second strands are not covalently linked to each other;

at least a portion of the first strand being complementary to the target RNA,

said target RNA thereby being modified.

95-96. (cancelled).

97. (previously presented) The method of claim 94 wherein a plurality of target RNAs are modified.

98. (previously presented) The method of claim 94 wherein said modification is characterized by cleavage of said target RNA.

99. (previously presented) The method of claim 94 wherein said cleavage is in vitro.

100. (previously presented) The method of claim 94 wherein the target RNA is present in a cell.

101-104. (cancelled).

105. (currently amended) A method of activating a nuclease activity within a cell comprising:

administering to the cell a double stranded RNA having first and second strands, said first strand comprising at least four consecutive 2'-hydroxyl ribonucleosides and at least one modified nucleoside;

the first and second strands being hybridized to each other, wherein the first and second strands are not covalently linked to each other;

at least a portion of the first strand being complementary to an RNA in the cell,

said nuclease activity thereby being activated.

106-107. (cancelled).

108. (previously presented) The method of claim 105 wherein the nuclease activity is characterized by the production of at least one cleavage product, said cleavage product containing a 3' terminal hydroxyl moiety.

109. (previously presented) The method of claim 105 wherein the nuclease activity is characterized by the production of at least one cleavage product, said cleavage product containing a 5' terminal phosphate moiety.

110. (previously presented) The method of claim 109 wherein said cleavage product further contains a 3' hydroxyl moiety.

111. (previously presented) The method of claim 105 wherein the nuclease activity is cleavage by a dsRNAse enzyme.

112-121. (cancelled).

122. (previously presented) The method of claim 121 wherein said modulation is in vitro.

123. (currently amended) A method of modulating the level of one or more target RNA comprising contacting the target RNA with a double stranded RNA having first and second strands, said first strand comprising at least four consecutive 2'-hydroxyl ribonucleosides and at least one modified nucleoside;

the first and second strands being hybridized to each other, wherein the first and second strands are not covalently linked to each other;

at least a portion of the first strand being complementary to the target RNA, said level of target RNA thereby being modulated.

124. (cancelled).

125. (currently amended) A method of eliciting a dsRNAse response in a cell comprising administering to said cell a double stranded RNA having first and second strands, said first strand comprising at least four consecutive 2'-hydroxyl ribonucleosides and at least one modified nucleoside;

the first and second strands being hybridized to each other, wherein the first and second strands are not covalently linked to each other;

at least a portion of the first strand being complementary to the target RNA, said dsRNAse response thereby being elicited.

126. (previously presented) The method of claim 124 or 125 wherein said dsRNase response is elicited in vitro.

127-157. (cancelled).

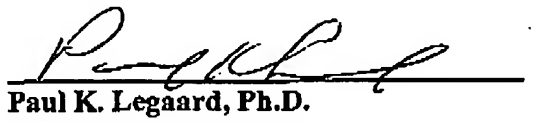
158. (currently amended) A method of modifying a target RNA comprising contacting said target RNA with a double-stranded oligomeric compound having first and second strands and wherein at least one of said first and said second strands includes a portion having four consecutive 2'-hydroxy ribonucleotides, wherein the first and second strands are not covalently linked to each other, and wherein at least one of said first and said second strands includes at least one peptide nucleic acid.

159-164. (cancelled).

DOCKET NO.: ISIS0002-103 (ISIS-5027) **PATENT**

In view of the foregoing, Applicant respectfully submits that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicant's undersigned representative at (215) 665-6914 if there are any questions regarding Applicant's claimed invention.

Respectfully submitted,



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